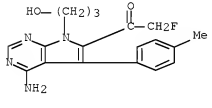
L5 ANSWER 1 OF 5 CAPLUS COPYRIGHT 2008 ACS on STN
AN 2007:1069336 CAPLUS Full-text
DN 147:499996
TI FGFR3 activates RSK2 to mediate hematopoietic transformation through tyrosine phosphorylation of RSK2 and activation of the MEK/ERK pathway
AU Kang, Sumin; Dong, Shaozhong; Gu, Ting-Lei; Guo, Ailan; Cohen, Michael S.; Lonial, Sagar; Khoury, Hanna Jean; Fabbro, Doriano; Gilliland, D. Gary; Bergsagel, P. Leif; Taunton, Jack; Polakiewicz, Roberto D.; Chen, Jing
CS Winship Cancer Institute, Emory University School of Medicine, Atlanta, GA, 30322, USA
SO Cancer Cell (2007), 12(3), 201-214
CODEN: CCAECI; ISSN: 1535-6108
PB Cell Press
DT Journal
LA English
AB To better understand the signaling properties of oncogenic FGFR3, we performed phospho-proteomics studies to identify potential downstream signaling effectors that are tyrosine phosphorylated in hematopoietic cells expressing constitutively activated leukemogenic FGFR3 mutants. We found that FGFR3 directly tyrosine phosphorylates the serine/threonine kinase p90RSK2 at Y529, which consequently regulates RSK2 activation by facilitating inactive ERK binding to RSK2 that is required for ERK-dependent phosphorylation and activation of RSK2. Moreover, inhibition of RSK2 by siRNA or a specific RSK inhibitor fmk effectively induced apoptosis in FGFR3-expressing human t(4;14)-pos. multiple myeloma cells. Our findings suggest that FGFR3 mediates hematopoietic transformation by activating RSK2 in a two-step fashion, promoting both the ERK-RSK2 interaction and subsequent phosphorylation of RSK2 by ERK.
IT 821794-92-7
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(Fmk as a first generation RSK inhibitor shows promising but so far limited effectiveness in treatment of FGFR3-expressing myeloma cells)
RN 821794-92-7 CAPLUS
CN Ethanone, 1-[4-amino-7-(3-hydroxypropyl)-5-(4-methylphenyl)-7H-pyrrolo[2,3-d]pyrimidin-6-yl]-2-fluoro- (CA INDEX NAME)



RE.CNT 43 THERE ARE 43 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 2 OF 5 CAPLUS COPYRIGHT 2008 ACS on STN
AN 2007:382499 CAPLUS Full-text
DN 146:395261
TI Selective serine/threonine kinase inhibitors
IN Taunton, Jack; Cohen, Michael; Shokat, Kevan; Zhang, Chao
PA The Regents of the University of California, USA
SO PCT Int. Appl., 84pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2007038613	A2	20070405	WO 2006-US37699	20060926
	WO 2007038613	A3	20071122		
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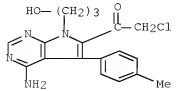
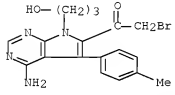
	RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AP, EA, EP, OA				
PRAI	US 2005-720902P	P	20050926		

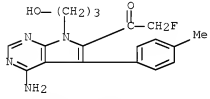
OS MARPAT 146:395261
AB Inhibition of protein kinases having one or more cysteine residues within the ATP binding site is effected by contacting the kinase, per se or in a cell or subject, with an inhibitory-effective amount of a compound having a heterocyclic core structure comprised of two or more fused rings containing at least one nitrogen ring atom, and an electrophilic substituent that is capable of reacting with a cysteine residue within the ATP binding site of a kinase. Preferred compds. include certain pyrrolopyrimidines and oxindoles having such an electrophilic substituent and optionally an aromatic or heteroarom. substituent that is capable of interacting with a threonine or smaller residue located in the gatekeeper position of the kinase. Kinases lacking such cysteine residues may be engineered or modified so that they are capable of being inhibited by such compds. by replacing a valine or other amino acid residue within the ATP binding site by a cysteine residue.
IT 821794-90-5
RL: PAC (Pharmacological activity); RCT (Reactant); THU (Therapeutic use); BIOL (Biological study); RACT (Reactant or reagent); USES (Uses)
(selective serine/threonine kinase inhibitors including pyrrolopyrimidines and oxindoles for prevention and treatment of cancer)
RN 821794-90-5 CAPLUS
CN Ethanone, 1-[4-amino-7-(3-hydroxypropyl)-5-(4-methylphenyl)-7H-pyrrolo[2,3-d]pyrimidin-6-yl]-2-chloro- (CA INDEX NAME)



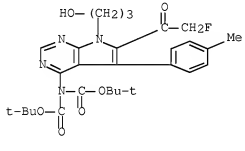
IT 821794-87-0P 821794-92-7P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)(selective serine/threonine kinase inhibitors including pyrrolopyrimidines and oxindoles for prevention and treatment of cancer)
RN 821794-87-0 CAPLUS
CN Ethanone, 1-[4-amino-7-(3-hydroxypropyl)-5-(4-methylphenyl)-7H-pyrrolo[2,3-d]pyrimidin-6-yl]-2-bromo- (CA INDEX NAME)



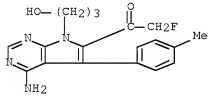
RN 821794-92-7 CAPLUS
CN Ethanone, 1-[4-amino-7-(3-hydroxypropyl)-5-(4-methylphenyl)-7H-pyrrolo[2,3-d]pyrimidin-6-yl]-2-fluoro- (CA INDEX NAME)



IT 932740-45-9P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(selective serine/threonine kinase inhibitors including pyrrolopyrimidines and oxindoles for prevention and treatment of cancer)
RN 932740-45-9 CAPLUS
CN Imidodicarbonic acid, N-[6-(2-fluoroacetyl)-7-(3-hydroxypropyl)-5-(4-methylphenyl)-7H-pyrrolo[2,3-d]pyrimidin-4-yl]-, C,C'-bis(1,1-dimethylethyl) ester (CA INDEX NAME)

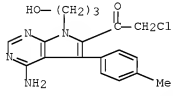


L5 ANSWER 3 OF 5 CAPLUS COPYRIGHT 2008 ACS on STN
AN 2007:171320 CAPLUS Full-text
DN 146:417272
TI A clickable inhibitor reveals context-dependent autoactivation of p90 RSK
AU Cohen, Michael S.; Hadjivassiliou, Haralambos; Taunton, Jack
CS Program in Chemistry and Chemical Biology, and Department of Cellular and Molecular Pharmacology, University of California, San Francisco, CA, 94158-2280, USA
SO Nature Chemical Biology (2007), 3(3), 156-160
CODEN: NCBABT; ISSN: 1552-4450
PB Nature Publishing Group
DT Journal
LA English
AB P90 ribosomal protein S6 kinases (RSKs) integrate upstream signals through two catalytic domains. Autophosphorylation of Ser386 by the regulatory C-terminal kinase domain (CTD) is thought to be essential for activation of the N-terminal kinase domain (NTD), which phosphorylates multiple downstream targets. We recently reported fmk, an irreversible inhibitor of the CTD of RSK1 and RSK2. Here we describe fmk-pa, a propargylamine variant that has improved cellular potency and a 'clickable' tag for assessing the extent and selectivity of covalent RSK modification. Copper-catalyzed conjugation of an azidoalkyl reporter (the click reaction) revealed that fmk-pa achieves selective and saturable modification of endogenous RSK1 and RSK2 in mammalian cells. Saturating concns. of fmk-pa inhibited Ser386 phosphorylation and downstream signaling in response to phorbol ester stimulation, but had no effect on RSK activation by lipopolysaccharide. RSK autoactivation by the CTD is therefore context dependent, which suggests that NTD and CTD inhibitors should have distinct physiol. effects.
IT 821794-92-7P
RL: BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(N-terminal kinase domain activates p90 ribosomal protein S6 kinase C-terminal domain through autophosphorylation at Ser323 and Ser236 residues)
RN 821794-92-7 CAPLUS
CN Ethanone, 1-[4-amino-7-(3-hydroxypropyl)-5-(4-methylphenyl)-7H-pyrrolo[2,3-d]pyrimidin-6-yl]-2-fluoro- (CA INDEX NAME)

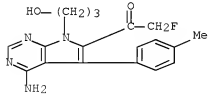


RE.CNT 31 THERE ARE 31 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 4 OF 5 CAPLUS COPYRIGHT 2008 ACS on STN
AN 2005:464185 CAPLUS Full-text
DN 143:168587
TI Structural Bioinformatics-Based Design of Selective, Irreversible Kinase Inhibitors
AU Cohen, Michael S.; Zhang, Chao; Shokat, Kevan M.; Taunton, Jack
CS Program Chemistry and Chemical Biology and Dep. Cellular and Molecular Pharmacology, Univ. California, San Francisco, CA, 94143-2280, USA
SO Science (Washington, DC, United States) (2005), 308(5726), 1318-1321
CODEN: SCIEAS; ISSN: 0036-8075
PB American Association for the Advancement of Science
DT Journal
LA English
AB The active sites of 491 human protein kinase domains are highly conserved, which makes the design of selective inhibitors a formidable challenge. We used a structural bioinformatics approach to identify two selectivity filters, a threonine and a cysteine, at defined positions in the active site of p90 ribosomal protein S6 kinase (RSK). A fluoromethylketone inhibitor, designed to exploit both selectivity filters, potently and selectively inactivated RSK1 and RSK2 in mammalian cells. Kinases with only one selectivity filter were resistant to the inhibitor, yet they became sensitized after genetic introduction of the second selectivity filter. Thus, two amino acids that distinguish RSK from other protein kinases are sufficient to confer inhibitor sensitivity.
IT 821794-90-5 821794-92-7
RL: BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)
(structural bioinformatics-based design of selective, irreversible inhibitors of p90 ribosomal protein S6 kinase (RSK) based on selectivity filters)
RN 821794-90-5 CAPLUS
CN Ethanone, 1-[4-amino-7-(3-hydroxypropyl)-5-(4-methylphenyl)-7H-pyrrolo[2,3-d]pyrimidin-6-yl]-2-chloro- (CA INDEX NAME)



RN 821794-92-7 CAPLUS
CN Ethanone, 1-[4-amino-7-(3-hydroxypropyl)-5-(4-methylphenyl)-7H-pyrrolo[2,3-d]pyrimidin-6-yl]-2-fluoro- (CA INDEX NAME)



RE.CNT 21 THERE ARE 21 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 5 OF 5 CAPLUS COPYRIGHT 2008 ACS on STN
AN 2005:14132 CAPLUS Full-text
DN 142:114090
TI A preparation of N-containing heterocyclic compounds, useful as selective serine/threonine kinase inhibitors
IN Taunton, Jack; Cohen, Michael; Shokat, Kevan; Zhang, Chao
PA The Regents of the University of California, USA
SO PCT Int. Appl., 70 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2005000197	A2	20050106	WO 2004-US11297	20040412
	WO 2005000197	A3	20050901		
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	RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	US 20070082884	A1	20070412	US 2005-552847	20051011
PRAI	US 2003-462554P	P	20030411		
	WO 2004-US11297	W	20040412		

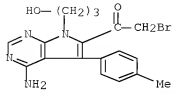
OS MARPAT 142:114090
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

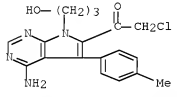
AB The invention relates to a preparation of N-containing heterocyclic compds., e.g. pyrrolopyrimidine derivs. of formula I [wherein: R1 is NH2, NH-heterocyclyl, or NH-aryl, etc.; R2 is (CH2)0-3R6; R6 is aromatic or (hetero)cyclic group; R3 and R4 are independently selected from H, aliphatic, aromatic, or heterocyclic group, etc.; R5 is H, alkyl- or aryl-substituted ether, thioether, or amine, etc.], useful as selective serine/threonine kinase inhibitors. Inhibition of protein kinases having one or more cysteine residues within the ATP binding site is effected by contacting the kinase, per se or in a cell or subject, with an inhibitory-effective amount of a compound having a heterocyclic core structure comprised of two or more fused rings containing at least one nitrogen ring atom, and an electrophilic substituent that is capable of reacting with a cysteine residue within the ATP binding site of a kinase. Kinases lacking such cysteine residues may be engineered or modified so that they are capable of being inhibited by such compds. by replacing a valine or other amino acid residue within the ATP binding site by a cysteine residue. For instance, pyrrolopyrimidine derivative II [Rsk2 inhibition (IC50, μM): WT - 0.015, C436V - >10, T439M - 3.4] was prepared via bromination of III by NBS, bromine/fluorine-exchange reaction of the obtained compound IV in the presence of KF, and subsequent hydrolysis (the yield of the exchange reaction was 40%).

IT 821794-87-0P 821794-90-5P 821794-92-7P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)(preparation of N-containing heterocyclic compds. useful as selective serine/threonine kinase inhibitors)

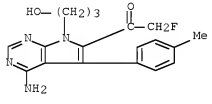
RN 821794-87-0 CAPLUS
CN Ethanone, 1-[4-amino-7-(3-hydroxypropyl)-5-(4-methylphenyl)-7H-pyrrolo[2,3-d]pyrimidin-6-yl]-2-bromo- (CA INDEX NAME)



RN 821794-90-5 CAPLUS
CN Ethanone, 1-[4-amino-7-(3-hydroxypropyl)-5-(4-methylphenyl)-7H-pyrrolo[2,3-d]pyrimidin-6-yl]-2-chloro- (CA INDEX NAME)



RN 821794-92-7 CAPLUS
CN Ethanone, 1-[4-amino-7-(3-hydroxypropyl)-5-(4-methylphenyl)-7H-pyrrolo[2,3-d]pyrimidin-6-yl]-2-fluoro- (CA INDEX NAME)



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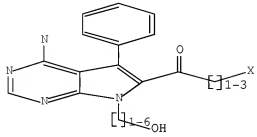


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L2              QUE L1
L3            0 S L2
L4            4 S L2 FUL

     FILE 'CAPLUS' ENTERED AT 15:14:02 ON 25 APR 2008
L5            5 S L4


COST IN U.S. DOLLARS                                SINCE FILE      TOTAL
                                                       ENTRY    SESSION
FULL ESTIMATED COST                                    28.21     206.78

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)          SINCE FILE      TOTAL
                                                       ENTRY    SESSION
CA SUBSCRIBER PRICE                                    -4.00      -4.00

STN INTERNATIONAL LOGOFF AT 15:15:30 ON 25 APR 2008
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